

# Oocyte cryopreservation for age-related fertility loss

Citation for published version (APA):

Dondorp, W., de Wert, G., Pennings, G., Shenfield, F., Devroey, P., Tarlatzis, B., Barri, P., & Diedrich, K. (2012). Oocyte cryopreservation for age-related fertility loss. *Human Reproduction*, 27(5), 1231-1237. <https://doi.org/10.1093/humrep/des029>

**Document status and date:**

Published: 01/05/2012

**DOI:**

[10.1093/humrep/des029](https://doi.org/10.1093/humrep/des029)

**Document Version:**

Publisher's PDF, also known as Version of record

**Document license:**

Taverne

**Please check the document version of this publication:**

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

**General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

[www.umlib.nl/taverne-license](http://www.umlib.nl/taverne-license)

**Take down policy**

If you believe that this document breaches copyright please contact us at:

[repository@maastrichtuniversity.nl](mailto:repository@maastrichtuniversity.nl)

providing details and we will investigate your claim.

# Oocyte cryopreservation for age-related fertility loss<sup>†</sup>

ESHRE Task Force on Ethics and Law, including, W. Dondorp<sup>1,\*</sup>, G. de Wert<sup>1</sup>, G. Pennings<sup>2</sup>, F. Shenfield<sup>3</sup>, P. Devroey<sup>4</sup>, B. Tarlatzis<sup>5</sup>, P. Barri<sup>6</sup>, and K. Diedrich<sup>7</sup>

<sup>1</sup>Department of Health, Ethics and Society, Research Institutes CAPHRI and GROW, Maastricht University, Maastricht, The Netherlands

<sup>2</sup>Department of Philosophy, University of Ghent, Blandijnberg 2, Gent 9000, Belgium <sup>3</sup>Reproductive Medicine Unit, Obstetric Hospital, 2nd Floor, University College Hospital Huntley Street, London WC1 6AU, UK <sup>4</sup>Centre for Reproductive Medicine, UZ Brussel, Brussels, Belgium

<sup>5</sup>Infertility and IVF Center, Geniki Kliniki, 2 Gravias Street 7th Floor, Thessaloniki 546 45, Greece <sup>6</sup>Servei de Medicina de la Reproducció, Departament d'Obstetrícia, Institut Universitari Dexeus, Ginecologia i Reproducció, Barcelona, Spain <sup>7</sup>Department of Obstetrics and Gynaecology, University of Lubeck, Ratzeburger Allee 160, D-23538 Lubeck, Germany

\*Correspondence address. E-mail: w.dondorp@maastrichtuniversity.nl

Submitted on January 3, 2012; resubmitted on January 3, 2012; accepted on January 10, 2012

**ABSTRACT:** The recent introduction of oocyte vitrification has significantly advanced the outcome of oocyte cryopreservation, leading to clinical results comparable to those achieved in IVF using fresh oocytes, as reported by experienced centres. This has led to new debate, both in the professional community and in society at large, about the acceptability of offering this technology to reproductively healthy women who want to cryopreserve their oocytes against the threat of time. Given the many demands calling for simultaneous realization in a relatively short period of their lives, many women who want to have children feel to be under considerable pressure. The option of oocyte cryopreservation may in fact give them more breathing space. In this document, it is concluded that the arguments against allowing this application of the technology are not convincing. The recommendations include the need for adequate information of women interested in oocyte cryopreservation, also in order to avoid raising false hopes. The message must remain that women's best chances of having a healthy child are through natural reproduction at a relative early age. Centres offering this service must have the necessary expertise to employ oocyte cryopreservation efficiently with the so far non-standardized protocols. As data about long-term safety is still lacking, centres also have a responsibility to contribute to the collection of these data.

**Key words:** oocyte cryopreservation / oocyte vitrification / fertility preservation / ethics / non-medical reasons

## Introduction

The recently established possibility of effectively cryopreserving functional oocytes through vitrification promises to revolutionize IVF practice. One new option is that of women using this technology to protect their reproductive potential against the threat of time. This document analyses the ethical arguments about the acceptability of this option. In an earlier statement the Task Force concluded that 'oocyte freezing for fertility preservation without a medical indication should not be encouraged' (Shenfield *et al.*, 2004). In the light of new scientific developments, and after considering relevant ethical arguments, the Task Force now takes the view that oocyte cryopreservation to improve prospects of future child bearing should also be available for non-medical reasons.

## Background and facts

### Effectiveness and safety of oocyte cryopreservation

The inefficiency of conventional slow-freezing techniques has for decades prevented the widespread implementation of oocyte cryopreservation in clinical practice. The introduction of oocyte vitrification significantly advanced the outcome of oocyte cryopreservation resulting in outcomes comparable to those achieved with fresh oocytes, as reported by experienced centres (Cobo *et al.*, 2010; Rienzi *et al.*, 2010). A large randomized clinical trial demonstrated that the effectiveness of vitrified oocytes is non-inferior to fresh oocytes in terms of ongoing pregnancy rates in an oocyte donation programme (Cobo *et al.*, 2010). Data from peer-reviewed literature conclude in

<sup>†</sup> ESHRE pages content is not externally peer-reviewed. The manuscript has been approved by the Executive Committee of ESHRE.

a 4–5% live birth rate per vitrified oocyte in women under the age of 36 years (Oktay et al., 2006; The Practice Committee of the SART and ASRM, 2008), meaning that one live birth is to be expected on average per 20–25 vitrified oocytes.

From the current data, it appears that vitrification is more efficient than slow freezing. Vitrification is achieved by combining a high concentration of cryoprotectants with high cooling and warming rates. Unlike slow freezing, vitrification results in the complete elimination of ice crystal formation avoiding the main cause of cryopreservation injury. These high cooling and warming rates are usually achieved by the use of open systems in which the samples are put into direct contact with liquid nitrogen during vitrification, allowing possible contamination. Aseptic modifications for open system vitrification, such as ultraviolet liquid nitrogen sterilization, have been described by Parmegiani et al. (2011) and recent observational data report highly efficient oocyte vitrification using high security closed vitrification devices (Stoop et al., 2011a).

In a recent systematic review of 22 observational studies examining the neonatal health of children born after slow freezing of oocytes (Wennerholm et al., 2009), the authors found limited information on birthweight or karyotype examinations and in most studies the only information given regarding childrens' well-being was 'healthy'. A large study by Chian et al., (2008) found reassuring evidence that pregnancies and infants conceived following oocyte vitrification are not associated with increased risk or adverse obstetric and perinatal outcomes. A literature review by Noyes et al. (2009), comprising all (900) verified live born infants resulting from assisted reproduction using cryopreserved oocytes, concluded that compared with naturally conceived infants, there was no difference in the rate of congenital anomalies. Although current data seem reassuring, there is no data available on the long-term child follow-up.

## Potential users' interest

Until now, only limited research has been done into attitudes towards oocyte cryopreservation for 'social reasons' among women of reproductive age. The outcomes of a recent Belgian study suggest that a significant proportion of young women would consider safeguarding their reproductive potential or are at least open to this idea (Stoop et al., 2011b).

## General ethical principles

### Beneficence

The principle of beneficence ('doing good') belongs to the Hippocratic core of medical ethics. It is traditionally related to an account of the good of medicine understood as preventing and curing disease (and caring for the ill). Reproductive medicine is widely regarded as fitting in with this medical model, even though many fertility treatments do not restore natural fertility but aim at avoiding the consequence (involuntary childlessness) of compromised reproductive functions. Other things being equal, fertility preservation for women at risk of disease related or iatrogenic premature menopause can be accounted for in terms of this model as an unproblematic instance of medical beneficence. But, what about fertility preservation for women who fear natural fertility loss? As female fertility loss around the age of 40–45 is a natural phenomenon, this application of the technology would

seem to fall outside the scope of the medical model. If so, should doctors not refrain from fulfilling such requests? There are two possible rejoinders to this. One is that the appeal to the traditional limits of the profession ignores that in reality the practice of medicine comprises many activities that would then also have to be questioned. In the field of reproduction, one may think of sterilization, abortion and donor insemination for single or lesbian women. If those activities are acceptable in principle, it is difficult to maintain that things would be different with regard to fertility preservation for non-medical reasons. The second, more fundamental, argument is that the appeal to the limits of medicine wrongly suggests that notions of health and disease can simply be inferred from facts about biological functioning without reference to socially mediated understandings (Richman, 2004). That this is not the case is quite obvious from the intractable nature of debates about whether and under what conditions infertility should be regarded as an instance of ill health. Moreover, certain accepted applications of reproductive medicine are better understood as a treatment for involuntary childlessness, period, regardless of whether this condition is the consequence of a biological or functional defect. IVF for 'idiopathic infertility' (currently one of the most frequent indications) is a good example. Under this heading, many couples are being treated whose subfertility is a consequence of natural ovarian ageing: the fact that the female partner has approached the end of her reproductive life span. If this is confirmed by a poor oocyte yield, many centres offer such couples the opportunity of IVF with donor oocytes, at least for a few more years. Nevertheless, these treatments are regarded as beneficence-based responses to a medical indication. This presupposes a wider understanding of reproductive health in the light of which fertility preservation for ovarian ageing cannot so easily be dismissed as a non-health-related preference.

### Respect for reproductive autonomy

Even when one accepts that a strict demarcation between medical and social needs cannot be drawn in the field of assisted reproduction, one may still ask whether fertility specialists should go along with all requests for fertility preservation. Fertility preservation for women at risk of disease related or iatrogenic premature menopause clearly falls within the scope of reproductive medicine. The same can arguably be said of fertility preservation for women who want to have children and are still without a partner at the age of 35. Their request is understandable, given that there is a reasonable chance beyond their own control that they will remain childless. But what about requests from women who deliberately choose to postpone childbearing while giving temporary priority to other life goals such as the build-up of a career? Can one still say in such cases that fertility preservation is needed to avoid involuntary childlessness? How involuntary would that condition be if it results from the woman's own choices? Instead of going along with such requests, should fertility specialists not simply tell these women to reconsider their priorities?

There are several problems with this view. For one thing, the suggestion that, in the case of the 'career woman', there is no real need for fertility preservation is psychologically questionable. It neglects the intrinsic connection between a person's most central life projects and his or her sense of identity and how this connection may present as a form of personal necessity (Williams, 1985). This means that the

postponement choices of the 'career women' need not make her eventual childlessness less involuntary. Moreover, it should be acknowledged that not yet having a partner with whom to have children may also be a consequence of a strong focus on one's career (Nekkebroeck *et al.*, 2010). This means that the two groups of possible beneficiaries referred to in this debate are overlapping rather than distinct and that the postponing 'career woman' is not so deviant a character as many seem to think. Postponement of childbearing is not a new phenomenon that only comes into play with the improvements in oocyte cryopreservation. In fact, it explains a large part of the current need for IVF. If one accepts to treat deliberate postponers, one should also help them to save their oocytes at an earlier age as a form of prevention. To the extent that concerns about this development are also about avoidable risks and costs, these issues will be discussed below. But the fact that, in this debate, there is much more sympathy with women who find themselves without a partner than with those who want to give priority to their career or other life plans, seems to point beyond such concerns about risks and costs to traditional beliefs regarding the proper place of childbearing in a woman's life. In a secular debate, the problem with arguing from views about 'the good life' is that they rest on religious or naturalistic presuppositions that not all participants necessarily share. As imposing such views on others is morally unacceptable, fertility specialists should leave it to the women themselves to make their own informed decisions about the need for fertility preservation. Indeed, doing so is in line with the ethical principle of respect for the autonomy of persons. It is accepted that competent persons have the right to make their own reproductive decisions, including whether to have children, with whom, how many, etc. It would seem that this also includes the right to decide about when to reproduce and what priority to give to childbearing in relation to other life plans.

## Non-maleficence

Obtaining oocytes for fertility preservation requires a medical procedure (ovarian stimulation, oocyte pick-up) that is burdensome for the woman and not entirely without risk of complications. Whether this is acceptable in view of the principle of non-maleficence ('first do no harm') depends on the proportionality of the necessary procedures. On the one hand, the risks of bleeding and infection are extremely small (Vercammen *et al.*, 2011) and the occurrence of the ovarian hyperstimulation syndrome is almost fully avoidable (Devroey *et al.*, 2011). In regular IVF, these procedural risks are regarded as clearly outweighed by the benefits of the treatment. In fertility preservation, on the other hand, it is far from certain that the woman will eventually use her cryopreserved oocyte reserve for reproduction. It should also be taken into account that a woman who at around 35 would want to have a reasonable number of oocytes cryopreserved will need to undergo several stimulation cycles. These are proportionality affecting considerations that should certainly be discussed with requesting women as part of proper counselling. However, the importance of keeping open the prospect of having children later in their lives, and how this weighs up to the burdens and risks of repeated stimulation and oocyte-pick up can only be determined individually by the women concerned. A paternalistic attitude from the physician should be rejected. That a fertility centre may

still decide not to start treatment for reasons of cost-effectiveness and scarcity of resources is a different matter.

Centres offering this service must have the necessary expertise to employ oocyte cryopreservation efficiently with the so far non-standardized protocols. If not, harm may be done to women who mistakenly expect to be able to use good quality oocytes for reproduction at a later time. Any burdens, risks and costs may then turn out to have been disproportional.

In the quoted study on a group of potential users, women referred to reproductive safety as a determining factor in their decision-making about fertility preservation (Stoop *et al.*, 2011b). The health of any future children born as a result of reproductive technologies should also be a paramount concern of fertility specialists and clinics (Pennings *et al.*, 2007). Although the number of children born from cryopreserved oocytes is still small, there is no indication that they would be at increased risk of adverse health outcomes. But more data are clearly needed. These should not only be based on short-term, but also on medium- and long-term follow-up of children. Centres offering this novel technology have a responsibility to contribute to the collection of these data (Dondorp and de Wert, 2011).

In the debate about fertility preservation for ovarian ageing, concerns have also been raised about possible risks of reproduction at a later age. One may think here not only of a higher risk of pregnancy complications, but also of putting the future child at risk of negative psychosocial consequences of having to grow up with older parents. Earlier, these same concerns have been raised with regard to IVF using donor oocytes in peri- and post-menopausal women. However, in well-selected healthy women pregnancy risks are not prohibitively higher up to the age of at least 50 (Sauer *et al.*, 1995; Sauer *et al.*, 1996; Paulson *et al.*, 2002; Chibber, 2005). With regard to the welfare of the child, helping older women to have children need not be irresponsible as long as at least one of the parents can be expected to remain healthy enough to meaningfully fulfill the parental role up until the child reaches adulthood (Health Council of the Netherlands, 1997). Moreover, older parents have some advantages (relational stability, parent-child interactions, financial situation, etc.) compared with younger parents (Pennings, 1995). Given that most women who want to have oocytes cryopreserved for later use aim to buy some extra years allowing them to have children in the early years of their fourth decade (Stoop *et al.*, 2011b), there is no unacceptable risk either for themselves or their future children.

Compared with current options of trying to get pregnant in the fourth decade, using one's own stored, young oocytes may in fact have important benefits for the women involved. Compared with IVF with donor oocytes, there is a clear benefit in the prospect of having a child that is genetically one's own. And compared with using one's own fresh but age-compromised oocytes, the benefits are a higher success rate and a lower rate of oocyte-related health risks for the offspring, especially chromosomal abnormalities.

## Justice and societal implications

In relation to the life expectancy of modern humans, women stand to lose their natural fertility at a relatively early age. Given the many demands calling for simultaneous realization in a relatively short period of their lives, many women who want to have children feel to be under considerable pressure. The option of oocyte

cryopreservation may give them more breathing space. For men, the combination of fatherhood with other life plans is not as difficult. Not only do they tend to leave most of the burdens of daily care to their partners, but they also have the opportunity to reproduce until much later in their lives. Moreover, men already can have their sperm cryopreserved. This is done for medical reasons, but sperm banking is also commercially available as a means of preserving reproductive capacity to men in jobs or sports that pose a possible threat to their fertility. From a feminist perspective, therefore, the availability of options for female fertility preservation can be regarded as an important step towards greater reproductive justice (Goold and Savulescu, 2009; Homburg et al., 2009).

Others have objected that as a solution to women's problems with having their children earlier in life, fertility preservation is a typical instance of 'medicalization': the tendency to seek medical answers to societal problems. The problem here is that many modern societies are organized in ways that make it difficult for women to have children at what would biologically be the best age for reproduction. According to these critics, offering fertility preservation to healthy women will lead to undermining efforts aimed at addressing the societal cause of the high maternity age, thus only reinforcing and perpetuating the problem. But however important it is to create better conditions for combining early childbearing with the pursuit of other life plans and also to educate young women that their chances of successful reproduction and healthy children are greatest when they start early, all this should not lead to ignoring the plight of those who find themselves caught in the trap of time. That, indeed, would be unjust. Moreover, there is no good reason for not doing both: stimulate early childbearing while allowing fertility preservation for those who need or want extra time.

The precise societal implications of fertility preservation for ovarian ageing not only depend on the number of women who will make use of this option, but also on how having a stored reserve will affect reproductive decisions and possible outcomes. Different scenarios need to be distinguished: (i) women who would otherwise have remained childless or who because of their age would have had no other option than reproduction with the use of donor oocytes can still have their genetically related child (or children); (ii) women who would otherwise have used their last chance of having a child through IVF with their own fresh oocytes can use their (biologically younger) cryopreserved oocytes instead, thereby enlarging their chances of success and reducing the risk of having a child with a chromosomal abnormality and (iii) women who would otherwise have had their children at an age where natural conception was still possible can choose to postpone childbearing until after the loss of natural fertility.

It is important to note that only the last of these scenarios involves what the critics of this development seem to fear, namely that (relatively) early and natural reproduction will come to be replaced by assisted reproduction at a later stage in women's lives. This indeed entails higher costs and a higher complication rate and may also lead to a higher rate of involuntary childlessness than would otherwise have been the case. However, the comparison presupposes that natural reproduction would have been a realistic option for the women involved. Where this is not the case, the other scenarios show that the option of using a cryopreserved reserve may in fact bring important benefits, not just to individual women (and their

partners) but also to society. Societal benefits include the birth of additional children at a time of declining population birth rates in developed countries, a lower dependency on the use of donor oocytes (avoiding extra costs and psychosocial complications) and more cost-effective IVF in older women, with a lower rate of chromosomal abnormalities (Mertes and Pennings, 2012).

A further scenario is that of women cryopreserving a sufficient number of oocytes for later but without ever using this reserve, either because they find a partner when natural reproduction is still possible, or because they decide not to have children after all. For the women involved an important benefit may still be that having a stored, healthy oocyte reserve takes away much of the time pressure both on creating the conditions for starting a family, including courtship, and on the realization of other life plans. Moreover, left-over oocytes can still be used for donation either for infertility treatment or for scientific research. In fact, the greater availability of donor oocytes promises to be an important societal advantage of this development.

## Specific ethical considerations

### Informed decision-making

When offering oocyte cryopreservation for age-related fertility loss, professionals and clinics should avoid presenting this option as a warrant for successful future reproduction (Harwood, 2009). Fertility preservation should be discussed for what it is: an emergency measure for women who fear not to be able to have their children before running out of functional oocytes. Having a stored reserve will give them the prospect of a limited number of IVF cycles at a later stage of their life, which may or may not lead to a child. In order to avoid raising false hopes, professionals should tell women that their best chances of having a child are through natural reproduction at a relative early age. It would also be relevant for them to know the percentage of women who eventually make no use of their stored reserve.

Women interested in oocyte cryopreservation should be adequately informed about the nature, burdens and risks of the procedure, the conditions under which their oocytes can be stored, the time frame within which they can be used, and the costs of procedure, storage and use. They should also be provided with an estimate of their chances of successful reproduction. This requires state of the art data about the expected oocyte yield per stimulation cycle and the percentage of life-born children per cryopreserved oocyte, stratified for women of different ages and with different ovarian reserve test results, taking account of the literature regarding the use of specific cryopreservation techniques (like vitrification or slow freezing). This information should also relate to the expertise and efficiency of the centre. Women should be informed that oocyte cryopreservation is a relatively new technology, that the number of children born from such oocytes is still limited and that follow-up data regarding any possible offspring health risks are still being collected.

As a precondition for informed decision-making, women interested in oocyte cryopreservation should be made aware of the possibility of considering alternatives with different profiles of advantages and disadvantages. This not only includes the future use of donor oocytes but also alternative forms of fertility preservation, e.g. involving cryopreservation of ovarian tissue or embryos. The former of these



approaches has the theoretical advantage of making a larger number of oocytes available for postponed reproduction. However, this approach to fertility preservation has also been introduced relatively recently and the number of children born is still very limited. Embryo cryopreservation has the advantage of being an established technology, but this approach would seem to be interesting only for women in a stable relationship (Dondorp and De Wert, 2009).

## Age limits

Women interested in fertility preservation should be advised that the cryopreservation procedure should ideally be done at a relatively early age and if possible prior to the age of 35, being the age limit generally used for oocyte donor recruitment. Although cryopreservation for women >38 should not be recommended, there may be cases where a prior assessment of the ovarian reserve justifies the procedure. Counselling based on an individual assessment of the available reproductive potential would seem to be the best approach. At present, the average age of women deciding to save their oocytes for later is 38 (Gold *et al.*, 2006; Klein *et al.*, 2006; Sage *et al.*, 2008).

With regard to the time frame for using one's stored reserve, setting an age limit at around 50 would seem to be justifiable in the light of considerations already referred to. It could be argued that for women with a younger partner the line may be drawn higher, as there would then be at least one parent who can be expected to be able to guide the child into adulthood. In any case, however, there is no good reason for drawing a line here that is different from that regarding IVF using donor oocytes.

## Coverage

In countries where assisted reproduction is (partly) covered within the healthcare system, the question will arise who should pay for fertility preservation for ovarian ageing. A distinction should be made between the stages of stimulation and cryopreservation on the one hand, and that of reproduction (use) on the other. With regard to the reproduction stage, it seems clear that women who are no longer able to conceive naturally but who have a stored oocyte reserve that they want to use in IVF treatment would be eligible to have that treatment funded on conditions that are the same as those that currently hold for other fertility patients. Depending on those conditions, coverage should be expected for reproduction until the woman has reached the early years of her fourth decade. With regard to reimbursing treatment of women after that age, further debate will be necessary. As natural childbearing becomes more exceptional later in the fourth decade, many will find it less obvious that society should pay. On the other hand, it can be questioned whether this appeal to 'normal species functioning' should indeed determine the scope for reimbursement of assisted reproduction. A more practical consideration is that countries are already struggling to accommodate present IVF demand in healthcare budgets that are increasingly strained. Still, in many western societies, there are demographic reasons for welcoming the birth of any extra child born to women who are socially, economically and physically able to give it a good start in life.

With regard to the creation and preservation stages, it would seem logical to expect women to pay for this themselves. After all, they are reproductively healthy and, unlike women facing premature pathogenic or iatrogenic fertility loss, there is no obvious medical reason behind

their request. If society does not pay for elective procedures such as sterilization, why should it pay for fertility preservation? One important difference is that fertility preservation may be seen as a preventative measure with the same aim as assisted reproduction: avoiding unwanted childlessness. But even if in theory there might be arguments for reimbursing women who decide to cryopreserve their oocytes for later, these are considerably weakened from a cost-effectiveness perspective if it turns out that many or even most of these oocytes will not be used for reproduction. This includes both the use for the women themselves and the use by others when any left-over oocytes are subsequently destined for donation to others.

Still, many of those who will eventually use their stored reserve can be expected to do so at an age when assisted reproduction for women no longer able to conceive naturally is still covered by the healthcare system of their countries. In that situation, the fact that the first and most expensive stage of IVF treatment (obtaining mature oocytes through hormone stimulation) has already been done as part of the fertility preservation procedure significantly reduces the costs to the system, in addition to the clear benefits associated with the use of a woman's own younger oocytes. Against this background, it has been asked whether it is fair that women who chose to undergo the first stage of IVF treatment already at a younger age would not have this part of the procedure reimbursed if at a later moment in their lives they return for completing the treatment (Stoop, 2010). Proposals to mend this injustice include the offer of a refund if the woman's stored oocytes are effectively used for reproduction (either by the woman herself or through donation), and the offer of additional reimbursed transfer cycles (Mertes and Penning, 2012).

## Cryopreservation and donation

A new question arising with this development is what to do with left-over oocytes. As with embryos, the possibilities are donation for reproduction, donation for scientific research and destruction. Women should be informed about these options prior to cryopreservation and be asked to decide on what will happen in case they die or lose the ability to decide for themselves.

Unless helping a family member or friend is envisaged, most centres will only use oocytes for donation that were obtained before age 35. This means that women considering donation also as a means to have part of their investment refunded in case they would not need the oocytes themselves should be aware that this will only be possible if they decide to preserve their oocytes at a relatively early age.

Donation of a limited number of oocytes may also take place in the context of a 'freeze and share' arrangement as developed by a British fertility centre (Atalla, 2008). Under this arrangement women (under 35 and screened for being in good reproductive shape) do not have to pay for stimulation, harvesting and the first years of storage in exchange for donating half of their oocytes to the programme. The structure of this arrangement is similar to that of existing 'egg-sharing' programmes where women get free IVF treatment in exchange for part of their oocytes. Arrangements of this type have been criticized for introducing a covert form of payment for gametes, thus undermining the ideal of altruistic donation. However, altruistic donation should not be regarded as an end in itself. Donation in exchange for something of value to the donor does not as such constitute a moral

problem. Ethical concerns only arise when donation arrangements provide a context of exploitation. Although egg-sharing arrangements are not necessarily exploitative, there is certainly reason to critically review the conditions set by centres offering this type of service. Women should be fully informed about all relevant aspects of the arrangement, including the fact that by relinquishing their oocytes, they will become donors. They should be fully counselled about what it may mean for them to take that step.

## Recommendations

- (i) Oocyte cryopreservation should not just be available for women at risk of premature pathogenic or iatrogenic fertility loss, but also for those who want to protect their reproductive potential against the threat of time.
- (ii) Fertility specialists should refrain from passing judgement on a woman's motives for postponing childbearing and requesting fertility preservation.
- (iii) Centres offering this service must have the necessary expertise to employ oocyte cryopreservation efficiently. As data about long-term safety are still lacking, centres also have a responsibility to contribute to the collection of these data.
- (iv) Fertility specialists should be careful not to raise false hopes. Women interested in oocyte cryopreservation for age-related fertility loss should be told that their best chances of having a child are through natural reproduction at a relative early age. Fertility preservation should be presented as a preventative measure for those needing or wanting more time that increases their chances but offers no guarantee of success.
- (v) Interested women should be provided with a personalized and evidence-based estimate of the number of oocytes (and cycles) they would need for successful reproduction. This information should also relate to the expertise and efficiency of the centre. Although cryopreservation for women >38 should not be recommended, there may be cases where a prior assessment of the ovarian reserve justifies the procedure.
- (vi) Interested women should be adequately informed about all relevant aspects of the procedure for obtaining the oocytes, the conditions for storage, time frame for reproductive use and the options for deciding about the eventual fate of any left-over oocytes.
- (vii) Interested women should be informed that oocyte cryopreservation is a relatively new technology, that the number of children born from such oocytes is still limited and that long-term safety is still to be proved.
- (viii) More data are needed about the psychosocial aspects of fertility preservation for ovarian ageing, including women's motives for choosing this option, what it means for women to have a stored reserve and the choices they make regarding the use of this reserve.
- (ix) Policy-makers in countries where IVF is (partly) covered within the healthcare system should consider how women whose stored oocytes are eventually used for reproduction can be compensated.
- (x) Women embarking on 'freeze and share' arrangements should be fully counselled about the psychosocial implications of becoming an oocyte donor.
- (xi) The professions in the field of medically assisted reproduction should promote and contribute to societal efforts aimed at raising awareness of age-related female fertility decline among women and men of reproductive age.

## Acknowledgement

The Task Force acknowledges the expert advice obtained from D. Stoop, Centre for Reproductive Medicine, Free University of Brussels, Belgium.

## Funding

This work was funded by the European Society of Human Reproduction and Embryology (ESHRE).

## Conflict of interest

None declared.

## References

- Atalla N. 'Freeze and share': an evolution of egg-sharing. *BioNews* 2008;**476**, [http://www.bionews.org.uk/page\\_38016.asp](http://www.bionews.org.uk/page_38016.asp) (last accessed on 8 February 2012).
- Chian R, Huang J, Tan S, Lucena E, Saa A, Rojas A, Ruvalcaba Castellón LA, García Amador MI, Montoya Sarmiento JE. Obstetric and perinatal outcome in 200 infants conceived from vitrified oocytes. *Reprod BioMed Online* 2008;**16**:608–610.
- Chibber R. Child-bearing beyond age 50: pregnancy outcome in 59 cases 'a concern?'. *Arch Gynecol Obstet* 2005;**271**:189–194.
- Cobo A, Meseguer M, Remohi J, Pellicer A. Use of cryo-banked oocytes in an ovum donation programme: a prospective, randomized, controlled, clinical trial. *Hum Reprod* 2010;**25**:2239–2246.
- Devroey P, Polyzos NP, Blockeel C. An OHSS-free clinic by segmentation of IVF treatment. *Hum Reprod* 2011;**26**:2593–2597.
- Dondorp WJ, De Wert GM. Fertility preservation for healthy women: ethical aspects. *Hum Reprod* 2009;**24**:1779–1785.
- Dondorp W, de Wert G. Innovative reproductive technologies: risks and responsibilities. *Hum Reprod* 2011;**26**:1604–1608.
- Gold E, Copperman K, Witkin G, Jones C, Copperman AB. P-187: a motivational assessment of women undergoing elective egg freezing for fertility preservation. *Fertil Steril* 2006;**86**:S201.
- Goold I, Savulescu J. In favour of freezing eggs for non-medical reasons. *Bioethics* 2009;**23**:47–58.
- Harwood K. Egg freezing: a breakthrough for reproductive autonomy?. *Bioethics* 2009;**23**:39–46.
- Health Council of the Netherlands. In vitro fertilization. Publication number 1997/3E. The Hague: Health Council of the Netherlands, 1997.
- Homburg R, Van der Veen F, Silber SJ. Oocyte vitrification—women's emancipation set in stone. *Fertil Steril* 2009;**91**:1319–1320.
- Klein J, Howard M, Grunfeld L, Mukherjee T, Sandler B, Copperman AB. P-486: preliminary experience of an oocyte cryopreservation program: are patients presenting too late?. *Fertil Steril* 2006;**86**:S315.
- Mertes H, Pennings G. Elective oocyte cryopreservation: who should pay?. *Hum Reprod* 2012;**27**:9–13.
- Nekkebroeck J, Stoop D, Devroey P. O-036 A preliminary profile of women opting for oocyte cryopreservation for non-medical reasons. *Hum Reprod* 2010;**25**:i15–i16.

- Noyes N, Porcu E, Borini A. Over 900 oocyte cryopreservation babies born with no apparent increase in congenital anomalies. *Reprod Biomed Online* 2009;**18**:769–776.
- Oktaý K, Aylin P, Bang H. Efficiency of oocyte cryopreservation: a meta-analysis. *Fertil Steril* 2006;**86**:70–80.
- Parmegiani L, Cognigni GE, Bernardi S, Cuomo S, Ciampaglia W, Infante FE, Tabarelli de Fatis C, Arnone A, Maccarini AM, Filicori M. Efficiency of aseptic open vitrification and hermetical cryostorage of human oocytes. *Reprod BioMed Online* 2011;**23**:505–512.
- Paulson RJ, Boostanfar R, Saadat P, Mor E, Tourgeman DE, Slater CC, Francis MM, Jain JK. Pregnancy in the sixth decade of life: obstetric outcomes in women of advanced reproductive age. *JAMA* 2002;**288**:2320–2323.
- Pennings G. Age and assisted reproduction. *Int J Med Law* 1995;**14**:531–541.
- Pennings G, De Wert G, Shenfield F, Cohen J, Tarlatzis B, Devroey P. ESHRE Task Force on Ethics and Law 13: the welfare of the child in medically assisted reproduction. *Hum Reprod* 2007;**22**:2585–2588.
- Richman KA. *Ethics and the Metaphysics of Medicine. Reflections on Health and Beneficence*. Cambridge, MA: The MIT Press, 2004.
- Rienzi L, Romano S, Albricci L, Maggiulli R, Capalbo A, Baroni E, Colamaria S, Sapienza F, Ubaldi F. Embryo development of fresh 'versus' vitrified metaphase II oocytes after ICSI: a prospective randomized sibling-oocyte study. *Hum Reprod* 2010;**25**:66–73.
- Sage CFF, Kolb BM, Treiser SL, Silverberg KM, Barritt J, Copperman AB. Oocyte cryopreservation in women seeking elective fertility preservation—a multicenter analysis. *Obstet Gynaecol* 2008;**111**:205.
- Sauer MV, Paulson RJ, Lobo RA. Pregnancy in women 50 or more years of age: outcomes of 22 consecutively established pregnancies from oocyte donation. *Fertil Steril*. 1995;**64**:111–115.
- Sauer MV, Paulson RJ, Lobo RA. Oocyte donation to women of advanced reproductive age: pregnancy results and obstetrical outcomes in patients 45 years and older. *Hum Reprod* 1996;**11**:2540–2543.
- Shenfield F, Pennings G, Cohen J, Devroey P, Sureau C, Tarlatzis B. ESHRE Task Force on Ethics and Law 7: ethical considerations for the cryopreservation of gametes and reproductive tissues for self use. *Hum Reprod* 2004;**19**:460–462.
- Stoop D. Social oocyte freezing. *F, V and V in ObGyn* 2010;**2**:31–34.
- Stoop D, De Munck N, Jansen E, Platteau P, Van den Abbeel E, Verheyen G, Devroey P. Clinical validation of a closed vitrification system in an oocyte donation programme. *Reprod BioMed Online* 2011a. doi: 10.1016/j.rbmo.2011.10.015 (published online 4 November 2011).
- Stoop D, Nekkebroeck J, Devroey P. A survey on the intentions and attitudes towards oocyte cryopreservation for non-medical reasons among women of reproductive age. *Hum Reprod* 2011b;**26**:655–661.
- The Practice Committee of the Society for Assisted Reproductive Technology (SART) and the Practice Committee of the American Society for Reproductive Medicine (ASRM). Essential elements of informed consent for elective oocyte cryopreservation: a Practice Committee opinion. *Fertil Steril* 2008;**90**:S134.
- Vercammen L, Stoop D, De Vos M, Polyzos NP, Nekkebroeck J, Devroey P. Oocyte donation does not affect future reproductive outcome, a follow-up study. In: *ESHRE Annual Meeting*, Stockholm, July, 2011.
- Wennerholm U-B, Söderström-Anttila V, Bergh C, Aittomäki K, Hazekamp J, Nygren KG, Selbing A, Loft A. Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data. *Hum Reprod* 2009;**24**:2158–2172.
- Williams B. *Ethics and the Limits of Philosophy*. London: Fontana Press, 1985.